The reaction of 2-chloro-1-methoxynaphthalene and 2-anthracene forming conditions: convenient synthesis of annular polycyclic aromatic compounds

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Abstract
2-Bromobiphenylene and 2-chloro-1-methoxynaphthalene react with 3-cyanophthalides in the presence of LDA or LiTMP to give functionalized benzo[3,4]cyclobuta[1,2-b]anthracene-6,11-diones and naphthacene-5,12-diones, respectively.

Keywords: 2,3-Dehydronaphthalene, benzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione, LDA, LiTMP, cycloadditions

Introduction
Biphenylenes have recently been studied extensively because they can serve as a unit of new carbon allotropes and can function as spacers and building blocks for functionalized organic materials. One of the more important synthesis of functionalized biphenyls involves the intramolecular coupling of benzoannulated zincacyclopentadiene intermediates prepared from 2,2'-diaryls with ZnCl₂. During the course of our studies on the synthetic use of aryne reactions, we have prepared a wide variety of functionalized polycyclic quinones from the reaction of haloarenes with 3-lithiophthalides in the presence of sterically hindered bases such as LDA and LiTMP. It occurred to us that 2-bromobiphenylene might react similarly to give functionalized annulated biphenyls. Although 2-bromobiphenylene can in principal give two benzyne, i.e. 1,2-dehydro and 2,3-dehydrobiphenylene, our calculations have shown the 2,3-intermediate to be 4.47 kcal/mol more stable than the 1,2-isomer. The relative stability of 1,2 and 2,3-dehydrobiphenylenes were calculated with complete optimization of all geometric variables using the standard AM1 procedure incorporated in version 3.1 of Spartan Package. Furthermore, the latter being symmetric would give a single aryne product. Along similar lines, we decided to investigate also the reaction of 2-chloro-1-methoxynaphthalene with certain 3-cyanophthalides. The well-proven meta-directing effect of the methoxy group should also afford a single aryne product.
Results and Discussion

These expectations were indeed realized and are illustrated in Schemes 1 and 2. As shown in Scheme 1, 2-bromobiphenylene (2) and 3-cyanophthalides (3a-c) were treated with LDA and LiTMP to provide 2,3-dehydrobiphenylene (4) and the 3-lithio-3-cyanophthalides (5a-c), respectively. These intermediates then underwent cycloaddition to give the corresponding benzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione (6a-c) in 60-80% yields after usual workup. The benzyne precursor, 2-bromobiphenylene (2) was prepared by the bromination of biphenylene (1) with 1,8-diazabicyclo[5.4.0]undec-7-ene in the presence of HgCl2 in 75% yield. This method is superior to simple bromination which gives 2 in only 50% along with some polybromides. The 3-cyanophthalides (3a-c) were on hand from previous studies and IR spectra were consistent with proposed structures.

Scheme 1

As shown in Scheme 2, 1-methoxynaphthacene-(10a) and 1,3,6, trimethoxynaphthacene-5,12-dione (10b) were obtained in 75 and 87% yields, respectively, from the reaction of 2-chloro-1-methoxynaphthalene (7) and 3-cyanophthalides (3a and 3b). The regioselective
addition to 1-methoxy-2,3-dehydronaphthale (8) was clearly shown in the case of 5b to give a single adduct (9b). Obviously, no regiochemistry is involved in the case of the unsubstituted lithiated nitrile 5a. The IR, 1H NMR, 13C NMR, and mass spectra were consistent with proposed structures.

We next treated 7 with α-cyano-α-tolunitrile 11 and LDA expecting aryne 8 and α-lithio-α-cyano-α-tolunitrile (12) to undergo [2+4] cycloaddition to give the aminonaphthacene 13. However, as shown in Scheme 3, this reaction proceeded by a tandem addition-rearrangement pathway in which 8 and 12 reacted via a [2+2] cycloaddition pathway to the benzocyclobutonium adduct (14). Intermediate 14 then opened up to give the rearranged product, 2-cyano-3-(cyanobenzyl)-1-methoxynaphthalene (15) in 40% yield, after quenching.

Scheme 3

In conclusion, we have shown that 2,3-dehydrobiphenylene and 1-methoxy-2,3-dehydronaphthalene can serve as valuable intermediates in the synthesis of functionalized benzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione and naphthacene-5,12-dione, respectively.

Experimental Section

General Procedures. Melting points were taken on Fisher-Johns apparatus and are uncorrected. NMR spectra were recorded on a 400 MHz Brucker spectrometer: chemical shifts were related to TMS as internal standard. Chemicals were purchased from commercial sources. LDA and BuLi were purchased as solutions in hexanes. The glassware heated at 125 °C in oven overnight prior
to use. Benzyne reactions were done under an atmosphere of dry O2-free N2 contained in a balloon possessing a needle protruding through a rubber septum attached to one of the reaction flask necks.

Biphenylene (1), 2-bromobiphenylene (2) and 2-chloro-1-methynaphthalene (7) were prepared by literature procedures. The 3-cyanophthalides (3a-c) were available from previous studies.

**General procedure for the reaction of haloarenes (2 and 7) with 3-cyanophthalides (3a-c)**

In a flame-dried flask flushed with N2. LDA (15 mmol) was prepared by adding 6 mL of n-BuLi (2.5 M in hexanes) to a solution containing diisopropylamine (15 mg, 15 mmol) in THF (30 mL) at -70 °C. After stirring for 10 min, 5 mmol of the appropriate nitrile (3a-c) in 30 mL of THF was added and the temperature was allowed to warm to -40 °C. At this point, 5 mmol of the haloarene (2 or 7) in 30 mL of THF was added over a period of 20 min while maintaining the temperature between -30 to -40 °C. After the addition of the haloarene, the resulting mixture was allowed to warm to rt where it was stirred for an additional 3 h. The resulting dark reddish solution was quenched with 30 mL of saturated NH4Cl, and the solvent removed by rotary evaporation. The residue was extracted with three 20 mL portions of CH2Cl2. The fractions were combined, washed with 25 mL of 5% HCl, dried (Na2SO4) and concentrated (rotary evaporation) to provide a dark viscous liquid. The liquid was purified by flash chromatography (silica gel) using hexane/acetone (19:1) as eluent to give a solid product which was further purified by recrystallization from CH2Cl2-hexane. The physical properties of the products are given below.

**Benzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione (6a).** Yellow powder, mp 218-219 °C. IR (KBr) ν1684 cm-1. 1H NMR (CDCl3) δ 6.81 (d, J = 8.0 Hz, 2 H), 6.92 (m, 2 H), 7.32 (d, J = 8.0 Hz, 1 H), 7.73 (m, 2 H), 7.79 (d, J = 8.1 Hz, 1 H), 8.23 (m, 1 H), 8.32 (m, 1 H). 13C NMR (CDCl3) δ 119.2, 120.1, 121.9, 123.6, 126.8, 127.7, 130.8, 130.9, 131.0, 131.8, 133.7, 133.8, 134.1, 149.3, 151.1, 153.5, 158.2, 181.8, 182.2. Anal. Calcd for C20H10O2: C, 85.09; H, 3.57. Found: 85.15; H, 3.66.

**7-Methoxybenzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione (6b).** Yellow powder, mp 238-240 °C. IR (KBr) ν1667 cm-1. 1H NMR (CDCl3) δ 4.01 (s, 3 H), 6.91 (m, 4 H), 7.31 (d, J = 8.1 Hz, 1 H), 7.41(s, 1 H), 7.52 (s, 1 H), 7.7 (t, J = 8.1 Hz, 1 H), 7.94 (d, J = 8.1 Hz, 1 H), 8.2 (m, 1 H), 8.3 (m, 1 H). 13C NMR (CDCl3) δ 113.0, 113.9, 117.8, 119.6, 119.7, 119.8, 130.3, 130.4, 134.8, 135.2, 149.3, 149.6, 150.2, 157.3, 160.1, 171.2, 182.1, 182.9. Anal. Calcd for C21H12O3: C, 80.76; H, 3.87. Found: 80.87; H, 3.90.

**7,9-Dimethoxybenzo[3,4]cyclobuta[1,2-b]anthracene-6,11-dione (6c).** Yellow powder, mp 208-210 °C. IR (KBr) ν1682 cm-1. 1H NMR (CDCl3) δ 4.21 (s, 3 H), 7.82 (m, 4 H), 8.10 (m, 1 H), 8.33 (m, 2 H), 8.44 (m, 1 H), 8.70 (s, 1 H).
$^{13}$C NMR $\delta$ 63.0, 120.0, 124.7, 125.8, 127.0, 127.5, 129.5, 130.0, 130.3, 130.9, 132.0, 133.5, 133.6, 134.3, 135.9, 126.0, 160.0, 182.2, 183.2. Anal. Calcd for C$_{19}$H$_{12}$O$_3$: C, 79.16; H, 4.20. Found: C, 79.31; H, 4.26.

1,3,6-Trimethoxynaphthacene-5,12-dione (10b). Light yellow powder, mp 216-217 °C. IR (KBr) 1667. $^1$H NMR (CDCl$_3$) $\delta$ 3.91 (s, 3 H), 4.01 (s, 3 H), 4.12 (s, 3 H), 6.72 (d, $J = 4.2$ Hz, 1 H), 7.50 (d, $J = 4.1$ Hz, 1 H), 7.72 (m, 2 H), 8.13 (m, 1 H), 8.41 (m, 1 H), 8.58 (m, 1 H). $^{13}$C NMR (CDCl$_3$) $\delta$ 56.0, 56.6, 63.1, 103.1, 104.4, 116.7, 120.0, 124.5, 125.2, 128.9, 130.1, 131.1, 132.5, 136.3, 140.0, 159.2, 162.3, 164.9, 181.2, 182.4. Anal. Calcd for C$_{21}$H$_{16}$O$_3$: C, 72.41; H, 4.63. Found: C, 72.45; H, 4.70.

2-Cyano-3-(2-cynobenzyl)-1-methoxynaphthalene (15). Colorless crystals, mp 142-143 °C. IR (KBr) $\nu$ 2223 cm$^{-1}$. $^1$H NMR (CDCl$_3$) $\delta$ 4.21 (s, 3 H), 4.51 (s, 2 H), 7.30-7.80 (m, 8 H), 8.21 (d, $J = 8.1$ Hz, 1 H). $^{13}$C NMR (CDCl$_3$) $\delta$ 38.5, 63.0, 101.3, 113.1, 122.8, 124.2, 126.1, 127.0, 127.4, 127.8, 130.0, 130.2, 133.1, 133.2, 136.0, 136.4, 142.5, 162.5. Anal. Calcd for C$_{20}$H$_{14}$N$_2$O: C, 80.52, H, 4.73, N, 9.39. Found: C, 80.55; H, 4.74; N, 9.44.

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References and Notes